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1	IS&R	L1	1212	((347/40) or (347/21) or (347/48) or (347/68)).CCLS.	USPAT	2003/09/27 16:13
2	BRS	L2	315	1 and silicon	USPAT	2003/09/27 16:23
3	BRS	L3	1	5471232.pn.	USPAT	2003/09/27 16:24
4	BRS	L4	79	4680595.uref.	USPAT	2003/09/27 16:24
5	BRS	L5	72	4 not 2	USPAT	2003/09/27 16:25

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FILE 'CA' ENTERED AT 14:38:03 ON 27 SEP 2003
L1 291 S (MICRO OR NANO OR ARRAY OR PLATE)(2A)(DISPENSER OR MIXER)OR MICRODISPENSER OR NANODISPENSER
L2 36 S L1 AND PIEZO?
L3 42 S L1 AND(MICROMACHIN? OR MICROFABRICAT? OR(MACHIN? OR FABRICAT?)(1A)MICRO)
L4 37 S L1 AND (WAFER OR SILICON)
L5 79 S L2-4

=> d bib,ab 1-79

L5 ANSWER 17 OF 79 CA COPYRIGHT 2003 ACS on STN
AN 137:348548 CA
TI **Microdispenser** array for highly parallel and accurate liquid handling
AU Koltay, Peter; Steger, Reinhard; Birkle, G.; Huang, H.-C.; Sandmaier, Hermann; Zengerle, Roland
CS IMTEK, University of Freiburg, Freiburg, D-79110, Germany
SO Proceedings of SPIE-The International Society for Optical Engineering (2001), 4590(BioMEMS and Smart Nanostructures), 195-203
AB Liq. handling of vols. down to a few nanoliters is a key issue for modern bioanal. and pharmaceutical research and industry. In this paper we present a modular dispensing device for the highly accurate delivery of liqs. in the range of 10 nL - 500 nL at a precision of better than 5 % and a dosage rate up to 1000 nL/s. The reported dispensing technol. is based on a fast mech. displacement of liq. within a **micromachined silicon** chip (termed dosage chip). It overcomes limitations known from **piezo**-drop-on-demand dispensers or syringe-solenoid systems presently used in lab. automation. The accurate and very robust multi channel system which is modularly built out of individual dispensers is able to handle a variety of different liqs. simultaneously. A wide range of liqs. with different phys. properties can be handled with an up to now unequaled precision in that vol. range. The working principle of the device as well as newest characterization results are presented.

L5 ANSWER 25 OF 79 CA COPYRIGHT 2003 ACS on STN
AN 136:382513 CA
TI Clinically intelligent diagnostic devices and methods
IN Jacobs, Alice Anne; Nikolic, Boris; Gupta, Vineet
PA Genevention L.L.C., USA
SO PCT Int. Appl., 115 pp.
PI WO 2002042775 A2 20020530 WO 2001-US44868 20011127
PRAI US 2000-253284P P 20001127
AB The invention concerns the clin. intelligent design of diagnostic devices (such as microarrays) and methods of making and using such devices in differential diagnoses of specific clin. symptoms or sets of symptoms. In one aspect, the devices include various probes used to perform parallel screening of a no. of analytes. The probes are clustered on the devices based on known clin. presentations of symptoms assocd. with specific diseases and disorders. Diagrams describing the app. assembly and operation are given.

L5 ANSWER 38 OF 79 CA COPYRIGHT 2003 ACS on STN
AN 135:238925 CA
TI Multi-block lab-on-a-chip micro-arrays for biochemical analysis or synthesis
IN Geli, Francois

PA Fr.
SO PCT Int. Appl., 123 pp.
PI WO 2001070400 A1 20010927 WO 2001-FR881 20010322
PRAI FR 2000-3680 A 20000322
AB The invention concerns multi-block micro-arrays or macro-arrays incorporating labs. on chips, for use in chem., biochem. or biol. anal. or chem. or biochem. synthesis. It consists in a flat elementary module provided with parallel microchannels at their surface which emerge into the thickness and on the edge of their sides. The stacking of several similar flat elementary modules creates a sealed superimposition of lines of the micro-array or macro-array, and consequently an integral multi-block micro-array or macro-array. The microchannels can be provided with **micro-mixers** and widened portions, provided with mol.-fixing surfaces or receive micro-columns or micro-particles or micro-spheres, thereby enabling to perform on very small vols. parallel reactions, by juxtaposing the lines. Multi-block micro-arrays or macro-arrays can constitute an integrated chain of anal. or synthesis. Diagrams describing the app. assembly are given.

L5 ANSWER 40 OF 79 CA COPYRIGHT 2003 ACS on STN
AN 135:164258 CA
TI An automated and integrated protein workstation interfacing capillary HPLC with MALDI-TOF mass spectrometry using **piezoelectric** microdispensing
AU Miliotis, Tasso; Marko-Varga, Gyorgy; Nilsson, Johan; Laurell, Thomas
CS Department of Analytical Chemistry, Lund University, Lund, SE-221 00, Swed.
SO JALA (2000), 5(6), 93-95
AB A chip technol.-based workstation interfacing capillary liq. chromatog. to matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry, which can be operated in an unattended and fully automated mode, is described. The described microtechnol. platform is a simple way of interfacing microsepns. to MALDI-TOF mass spectrometry. The system can be automated to a high degree and an increased throughput in protein anal. may thus be obtained. Further optimizations of the microsystem will reduce total internal vols. and thus bring up sample throughput as well as lower detection levels.

L5 ANSWER 48 OF 79 CA COPYRIGHT 2003 ACS on STN
AN 133:290465 CA
TI Optimization of the droplet formation in a **piezoelectric** flow-through **microdispenser**
AU Nilsson, Johan; Bergkvist, Jonas; Laurell, Thomas
CS Department of Electrical Measurements, Lund Institute of Technology, Lund, SE-221 00, Swed.
SO Micro Total Analysis Systems 2000, Proceedings of the μTAS Symposium, 4th, Enschede, Netherlands, May 14-18, 2000 (2000), 75-78. Editor(s): Van den Berg, Albert; Olthuis, W.; Bergveld, Piet. Publisher: Kluwer Academic Publishers, Dordrecht, Neth.
AB Optimization of the droplet formation in a **silicon** based flow-through **microdispenser** is described. The effects discussed are satellite droplet formation and the oscillation of the liq. in the nozzle after droplet ejection. By controlling the shape of the pulse applied to the **piezoelec.** element, stable droplets can be generated without satellites. The vol. of the dispenser is 400 nL and 65 pL droplets are ejected from the 40 μm x 40 μm protruding nozzle.

L5 ANSWER 49 OF 79 CA COPYRIGHT 2003 ACS on STN
AN 133:275669 CA
TI An active **silicon** micromixer for μTAS applications
AU Woias, Peter; Hauser, Karin; Yacoub-George, Erwin

CS Fraunhofer-Institute for Integrated Circuits and Systems (IMS), Munich, D-80686, Germany
SO Micro Total Analysis Systems 2000, Proceedings of the μTAS Symposium, 4th, Enschede, Netherlands, May 14-18, 2000 (2000), 277-282. Editor(s): Van den Berg, Albert; Olthuis, W.; Bergveld, Piet. Publisher: Kluwer Academic Publishers, Dordrecht, Neth.
AB A novel **silicon** micromixer is presented, which was developed with special focus on the application in micro total anal. systems (μTAS). The device is based on an active mixing principle and uses a **silicon** chip with a thin **piezoelec**. actuated membrane as a key element. A small mixing chamber is formed between the membrane bottom and a chip carrier, which employs fluidic inlets and a common fluidic outlet to the chamber. The active micromixer was thoroughly studied concerning the mixing effect, the optimum operation set-point and the mixing efficiency. In contrary to static mixers it showed reliable mixing in a low flow range. This behavior was successfully demonstrated within a μTAS for colorimetric pH-detection.

L5 ANSWER 51 OF 79 CA COPYRIGHT 2003 ACS on STN
AN 133:275666 CA
TI A multi-nozzle **piezoelectric microdispenser** for improving the dynamic volumetric range of droplets
AU Stjernstrom, Marten; Rosengren, Lars; Holm, Johan; Vangbo, Mattias; Tormod, Stig
CS Amersham Pharmacia Biotech, Uppsala, Swed.
SO Micro Total Analysis Systems 2000, Proceedings of the μTAS Symposium, 4th, Enschede, Netherlands, May 14-18, 2000 (2000), 79-82. Editor(s): Van den Berg, Albert; Olthuis, W.; Bergveld, Piet. Publisher: Kluwer Academic Publishers, Dordrecht, Neth.
AB A **micromachined silicon** flow-through **microdispenser** was developed and evaluated. The reported device, designed for large vol. droplet ejection, was constructed in **silicon** by DRIE etching and **wafer** bonding techniques. The on-chip multi-orifice nozzle design allows the vol. range of the ejected droplets to be controlled by varying the no. of orifices in the nozzle. The authors assert a significant improvement of drop size achieved by changing to more nontrivial nozzle geometry.

L5 ANSWER 53 OF 79 CA COPYRIGHT 2003 ACS on STN
AN 133:55506 CA
TI Capillary liquid chromatography interfaced to matrix-assisted laser desorption/ionization time-of-flight mass spectrometry using an on-line coupled **piezoelectric** flow-through **microdispenser**
AU Miliotis, Tasso; Kjellstrom, Sven; Nilsson, Johan; Laurell, Thomas; Edholm, Lars-Erik; Marko-Varga, Gyorgy
CS Department of Analytical Chemistry, Lund University, Lund, SE-221 00, Swed.
SO Journal of Mass Spectrometry (2000), 35(3), 369-377
AB A **piezoelec**. flow-through **microdispenser** interfacing capillary liq. chromatog. (LC) with matrix-assisted laser desorption/ionization time-of-fight mass spectrometry (MALDI-TOF MS) was developed for the identification of biomols. The MALDI target plate was placed on a computer controlled high-resoln. x-y stage, on to which the column effluent was deposited as discrete spots, which thereby facilitated tracing of the chromatog. sepn. The entire target plate was sprayed with a homogeneous layer of α-cyano-4-cinnamic acid mixed with nitrocellulose by using an air-brush. Hence the tedious manual handling of a micropipetter applying matrix soln. on top of each fraction collected spot was avoided. The pre-made target plates were stable for at least 3 wk if kept in darkness at room temp., which easily allowed re-anal. of dispensed sample spots. The integrated microsystem was characterized and optimized by fluidics, dispersion, operational stability

and sensitivity parameters. The dispensing unit was developed specifically to match high-resoln. capillary LC sepns. using a dispenser with an internal vol. from inlet to the ejecting nozzle of 250 nL. Minimizing dead vols. was crucial to maintain the chromatog. resoln. The vol. of the ejected droplets was of the order of 60 pL. Successful sepns. of seven immunoregulating peptides were made: ACTH 1-17, bradykinin, enkephalin, angiotensin III, angiotensin II, angiotensin I and ACTH 18-39. Online sample dispensing on the target plate in combination with trace enrichment followed by automated MALDI-TOF MS identification is demonstrated, reaching a sensitivity of 100 amol.

L5 ANSWER 58 OF 79 CA COPYRIGHT 2003 ACS on STN
AN 132:119408 CA
TI Integrated Microanalytical Technology Enabling Rapid and Automated Protein Identification
AU Ekstroem, Simon; Oennerfjord, Patrik; Nilsson, Johan; Bengtsson, Martin; Laurell, Thomas; Marko-Varga, Gyoergy
CS Departments of Cell and Molecular Biology and Electrical Measurements, Lund University, Lund, 221 00, Swed.
SO Analytical Chemistry (2000), 72(2), 286-293
AB Protein identification through peptide mass mapping by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) has become a std. technique, used in many labs. around the world. The traditional methodol. often includes long incubations (6-24 h) and extensive manual steps. In an effort to address this, an integrated microanal. platform has been developed for automated identification of proteins. The **silicon micromachined** anal. tools, i.e., the microchip immobilized enzyme reactor (μ-chip IMER), the **piezoelec. microdispenser**, and the high-d. nanovial target plates, are the cornerstones in the system. The μ-chip IMER provides online enzymic digestion of protein samples (1 μL) within 1-3 min, and the **microdispenser** enables subsequent online picoliter sample prepn. in a high-d. format. Interfaced to automated MALDI-TOF MS, these tools compose a highly efficient platform that can analyze 100 protein samples in 3.5 h. Kinetic studies on the microreactors are reported as well as the operation of this microanal. platform for protein identification, wherein lysozyme, myoglobin, RNase A, and cytochrome c have been identified with a high sequence coverage (50-100%).

L5 ANSWER 62 OF 79 CA COPYRIGHT 2003 ACS on STN
AN 131:75329 CA
TI Components and systems for microliquid handling
AU Howitz, Steffen
CS GeSiM Gesellschaft fur Silizium-Mikrosysteme mbH, Rossendorfer Technologiezentrum, GroSSerkmannsdorf/Rossendorf, D-01454, Germany
SO BioMethods (Basel) (1999), 10(Microsystem Technology: A Powerful Tool for Biomolecular Studies), 31-73
AB A review, with 68 refs., of the title subject, including materials for manuf. of microfluidic components and techniques of manufg. microfluidic components and systems. Microfluidic components and systems described are manifolds, micropumps, **microdispensers**, micropipettes, microvalves, microinjectors, and micromixers.

L5 ANSWER 66 OF 79 CA COPYRIGHT 2003 ACS on STN
AN 130:176412 CA
TI **Micromachined** chemical fluid jet dispenser
IN Swierkowski, Steve P.
PA Regents of the University of California, USA
SO U.S., 9 pp.

PI US 5877580 A 19990302 US 1996-772639 19961223
PRAI US 1996-772639 19961223
AB A dispenser for chem. fluid samples that need to be precisely ejected in size, location, and time. The **dispenser** is a **micro**-electro-mech. systems (MEMS) device fabricated in a bonded Si **wafer** and a substrate, such as glass or Si, using integrated circuit-like fabrication technol. which is amenable to mass prodn. The dispensing is actuated by ultrasonic transducers that efficiently produce a pressure wave in capillaries that contain the chems. The 10-200 μm diam. capillaries can be arranged to focus in one spot or may be arranged in a larger dense linear array (.about.200 capillaries). The dispenser is analogous to some ink jet print heads for computer printers but the fluid is not heated, thus not damaging certain samples. Major applications are in biol. sample handling and in anal. chem. procedures such as environmental sample anal., medical lab. anal., or mol. biol. chem. expts.

L5 ANSWER 67 OF 79 CA COPYRIGHT 2003 ACS on STN
AN 130:35303 CA
TI Picoliter Sample Preparation in MALDI-TOF MS Using a **Micromachined Silicon** Flow-Through Dispenser
AU Oennerfjord, Patrik; Nilsson, Johan; Wallman, Lars; Laurell, Thomas; Marko-Varga, Gyoergy
CS Department of Analytical Chemistry, Lund University, Lund, 221 00, Swed.
SO Analytical Chemistry (1998), 70(22), 4755-4760
AB This paper presents a picoliter sample prepn. technique utilizing the flow-through principle, allowing online coupling of chromatog. systems to be made. The work was performed in order to investigate the characteristics and the physicochem. properties of the sample prepn. using typical mobile phase conditions from μ-CLC (column liq. chromatog.) sepns. The device presented here is a pressure pulse-driven dispenser, formed by two **silicon** structures processed by conventional **micromachining**. The pressure pulse is generated in the flow-through channel by a **piezoceramic** element. Depending on the orifice size, the droplets ejected range between 30 and 200 pL. The max. ejection frequency is 500 Hz, limited by resonances within the unit. A pyramid-shaped nozzle improves the directivity of the droplets since it reduces the wetting of the orifice front surface area. The risk of particles sticking close to the orifice is also minimized. The analyses of the deposited sample spots were carried out on a matrix-assisted laser desorption/ionization time-of-flight mass spectrometer with delayed extn. It was possible to detect attomole amts. (159-248 amol) of various proteins (cytochrome c, RNase A, lysozyme, and myoglobin) from a single droplet of matrix:analyte 1:1 (drop vol. ≈ 110 pL). Addnl., it was found that sample enrichment could be carried out using multiple depositions on the same spot; i.e., 31 nM of insulin was easily detected when more than four depositions were made on the same spot, while no detection was possible without sample enrichment. Size optimization of the MALDI sample spot gave target zones of 100-500-μm diam. that matched the size of the laser focal point and resulted in a considerably increased sample throughput.

L5 ANSWER 76 OF 79 CA COPYRIGHT 2003 ACS on STN
AN 127:308751 CA
TI **Micro-mixer** for handling of minute amounts of liquid
IN Howitz, Steffen; Wegener, Steffen
PA GeSim - Gesellschaft fuer Silizium-Mikrosysteme Mbh, Germany
SO Ger. Offen., 6 pp.
PI DE 19611270 A1 19970925 DE 1996-19611270 19960322
PRAI DE 1996-19611270 19960322
AB A **micro-mixer** consists of a micro-ejection pump contg. a pump chamber, a

micro-membrane provided with a **piezo**-elec. plate actuator, and an outlet channel with a discharge opening. The liqs. are (1) fed through sep. inlet channels into the outlet channel and/or pump chamber of the micro-ejection pump, (2) mixed before attaining the discharge opening, and (3) discharged in the form of drops. Typically, the inlet and outlet channels are in the form of capillaries. The app. is suitable for handling of liqs. in chem. anal., medicine, and biotechnol.

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